

Appl. No. : 09/991,721
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AMENDMENTS TO THE CLAIMS: NONE

1. **(Previously presented)** A composition of matter comprising a recombinant WR strain vaccinia virus, said vaccinia virus comprising a mutation in a thymidine kinase (TK) gene of the genome of said vaccinia virus to produce a negative TK phenotype and comprising a mutation in at least one vaccinia virus growth factor (VVGF) gene of the genome of said vaccinia virus to produce a negative VVGF phenotype.

2. **(Previously presented)** The composition of claim 1, wherein said vaccinia virus further comprises an exogenous nucleotide sequence.

3. **(Previously presented)** The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a deletion of nucleic acid sequence.

4. **(Previously presented)** The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus genome from which a thymidine kinase gene is deleted.

5. **(Previously presented)** The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing an insertion of nucleic acid sequence.

6. **(Previously presented)** The composition of claim 1, wherein said negative thymidine kinase phenotype results from a vaccinia virus thymidine kinase gene containing a substitution of nucleic acid sequence.

7. **(Previously presented)** The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a deletion of nucleic acid sequence.

8. **(Previously presented)** The composition of claim 7, wherein said deletion comprises a deletion of the EGF-receptor binding site of said vaccinia virus growth factor gene.

9. **(Previously presented)** The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from a vaccinia virus genome from which at least one vaccinia virus growth factor gene is deleted.

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10. **(Previously presented)** The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing an insertion of nucleic acid sequence.

11. **(Previously presented)** The composition of claim 1, wherein said negative vaccinia virus growth factor phenotype results from at least one vaccinia virus growth factor gene containing a substitution of nucleic acid sequence.

12. **(Previously presented)** The composition of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of tumor suppressor genes, cytotoxic genes, cytostatic genes, cytokines, suicide genes, and antigen encoding genes.

13. **(Previously presented)** The composition of claim 12, wherein said tumor suppressor gene is selected from the group consisting of WT1, p53, p16, Rb, and BRCA1.

14. **(Canceled)**

15. **(Previously presented)** The composition of claim 1, wherein said vaccinia virus is produced by a virus particle containing a virus genome, wherein expression of said genome produces a vaccinia virus with a negative thymidine kinase phenotype and a negative vaccinia virus growth factor phenotype.

16. **(Canceled)**

17. **(Previously presented)** The composition of claim 1, wherein said vaccinia virus is constructed such that the gene for *E. coli lacZ* is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

18. **(Previously presented)** The composition of claim 1, wherein said vaccinia virus is constructed such that the gene for enhanced green fluorescent protein (EGFP) is inserted into the thymidine kinase (TK) or virus growth factor (VGF) site.

19.-24 **(Canceled)**

25. **(Previously presented)** A product made by the method of:

providing a WR strain vaccinia virus genome and constructing a recombinant WR strain vaccinia virus by;

mutating at least one vaccinia virus growth factor gene of said vaccinia virus genome to produce a negative vaccinia virus growth factor phenotype; and

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mutating a thymidine kinase gene of said vaccinia virus genome to produce a negative thymidine kinase phenotype, whereby a recombinant WR strain vaccinia virus is constructed.

26-44. (Canceled)

45. (Previously presented) The composition of claim 2, wherein said exogenous nucleotide sequence is selected from the group consisting of cystic fibrosis transmembrane regulator (CFTR), Factor VIII, low density lipoprotein receptor, beta-galactosidase, alpha-galactosidase, beta-glucocerebrosidase, insulin, parathyroid hormone, and alpha-1-antitrypsin.

46. (Previously presented) The composition of claim 2, wherein said exogenous nucleotide sequence is introduced to inactivate said TK gene.

47. (Previously presented) The composition of claim 2, wherein said exogenous nucleotide sequence is introduced to inactivate said VVGF gene.

48. (Previously presented) The composition of claim 12, wherein said exogenous nucleotide sequence is a cytokine.

49. (Previously presented) The composition of claim 12, wherein said exogenous nucleotide sequence is a suicide gene.

50. (Previously presented) The composition of claim 2, wherein said exogenous nucleotide sequence is an imaging agent.